Application No. 09/937,191
Filed: January 3, 2002
TC Art Unit: 1642
Confirmation No.: 6276

AMENDMENT TO THE CLAIMS

1. (Currently Amended) A method of using ~~Utilization of~~ at least one aminopeptidase inhibitor for ~~the production of a medicament used in the~~ treatment of ~~very early stages of~~ tumor diseases, the method comprising:

providing a subject suffering from or thought to be at risk of suffering from a tumor disease; and ~~wherein the treated tumor is a primary tumor,~~

administering to the subject a medicament for treatment of a tumor disease, the medicament comprising an aminopeptidase inhibitor, whereby the ~~at least one~~ aminopeptidase inhibitor causes blocking of polarization of an invasive ~~human or animal~~ tumor ~~cells~~ cell by modifying at least one surface protein ~~CD13~~, wherein the surface protein is ~~as~~ a member of a protein network on the surface of the invasive tumor ~~cells~~ cell, ~~whereby~~ the protein network ~~comprises~~ comprising ~~up to 30 surface~~ proteins selected from the group consisting of CD4, CD8, HLA-DR, HLA-DQ, CD3, CD26, CD38, CD45RA, CD16, CD57, CD56, CD7, CD54, CD58, CD138, CD13, CD62L, CD71, CD11b, CD36, CD29, CD49d, CD18, CD49f, CD19, CD2, CD20, CD10, CD44 and CD80

~~1. CD4 2. CD8 3. HLA-DR 4. HLA-DQ 5. CD3~~
~~6. CD26 7. CD38 8. CD45RA 9. CD16 10. CD57~~
~~11. CD56 12. CD7 13. CD54 14. CD58 15. CD138~~
~~16. CD13 17. CD62L 18. CD71 19. CD11b 20. CD36~~
~~21. CD29 22. CD49d 23. CD18 24. CD49f 25. CD19~~
~~26. CD2 27. CD20 28. CD10 29. CD44 30. CD80~~.

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2. (Currently Amended) The ~~utilization as claimed in~~ method of claim 1, wherein ~~characterized in that said at least one~~ the aminopeptidase inhibitor is ~~an aminopeptidase inhibitor of the homophtalimide type~~ a homophthalimide, ~~and/or~~ an actinonin, ~~and/or~~ a bestatin, ~~and/or~~ an antibody~~, in particular a monoclonal antibody,~~ against one of said surface proteins or a combination thereof.

3. (Canceled)

4. (Currently Amended) The ~~utilization as claimed in~~ method of claim 1, wherein ~~characterized in that for producing said~~ the medicament further comprises~~,~~ an ~~at least one~~ additional inhibitor, the additional inhibitor inhibiting at least one member of the protein network, wherein the at least one member of the protein network ~~is used that inhibits at least one surface protein that~~ is not an aminopeptidase.

5. (Currently Amended) The ~~utilization as claimed in~~ method of claim 1, wherein ~~characterized in that said at least one~~ the aminopeptidase inhibitor ~~and/or at least one additional inhibitor~~ causes a modification of ~~at least one~~ a surface protein of the invasive ~~said~~ tumor ~~cells~~ cell, the ~~which~~ surface protein being ~~is~~ responsible for adhesion to an endothelial ~~cells~~ cell, ~~and/or~~ an extracellular ~~structures~~ structure~~, in particular organ specific endothelial cells and/or organ specific extracellular structures~~ or any combination thereof.

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6. (Currently Amended) The ~~utilization as claimed in~~ method of claim ~~1~~ 4, wherein ~~characterized in that said at~~ the ~~least one~~ aminopeptidase inhibitor, ~~and/or at least one~~ the additional inhibitor or a combination thereof ~~will cause~~ causes modification of ~~the~~ an ~~-~~adhesive ~~functions~~ function of at least one endothelial ~~cells~~ cell.

7. (Currently Amended) The ~~utilization as claimed~~ method of ~~in~~ claim ~~1~~ 4, wherein ~~characterized in that~~ the expression of ~~at least one~~ a surface protein~~, in particular of an adhesion molecule,~~ is ~~may be~~ influenced by ~~means of at least one~~ the aminopeptidase inhibitor, the ~~and/or at least one~~ additional inhibitor or a combination thereof.

8. (Canceled)

9. (Withdrawn) A method for identifying at least one aminopeptidase inhibitor that causes blocking of polarization of invasive human or animal tumor cells of a primary tumor created in the very early stages of tumor diseases, comprising:

a) detecting surface protein combinations of a protein network that are on the surface of the untreated tumor cells, whereby the protein network comprises up to 30 surface proteins selected from the group consisting of:

1. CD4	2. CD8	3. HLA-DR	4. HLA-DQ	5. CD3
6. CD26	7. CD38	8. CD45RA	9. CD16	10. CD57

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11. CD56	12. CD7	13. CD54	14. CD58	15. CD138
16. CD13	17. CD62L	18. CD71	19. CD11b	20. CD36
21. CD29	22. CD49d	23. CD18	24. CD49f	25. CD19
26. CD2	27. CD20	28. CD10	29. CD44	30. CD80;

b) treating said or similar tumor cells with at least one aminopeptidase inhibitor;

c) detecting said surface protein combinations of the protein network that are on the surface of the treated tumor cells; and

d) comparing the surface protein combinations detected in steps a) and c), whereby the at least one aminopeptidase inhibitor, if there is a divergence of the surface protein combinations detected in step a) from the surface protein combinations detected in step c) in that there is at least one modification of surface protein CD13, will cause blocking of polarization of said tumor cells.

10. (Withdrawn) The method as claimed in claim 9 characterized in that said method includes a further step, following step d), in which the at least one aminopeptidase inhibitor identified in step d) is added to at least one polarizing tumor cell and/or immune cell, and the further development of the at least one polarizing tumor cell and/or immune cell is detected.

11. (Withdrawn) The method as claimed in claim 9 characterized in that said method includes a further step, following step d), in which any binding of the untreated tumor cells to organ-specific endothelial cells and/or to organ-specific extracellular structures

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is detected, in which any binding of the tumor cells treated with the at least one aminopeptidase inhibitor identified in step d) to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

12. (Withdrawn) A method for identifying at least one inhibitor that in combination with at least one aminopeptidase inhibitor, will cause blocking of polarization of invasive human or animal tumor cells of a primary tumor created in the very early stages of tumor diseases, comprising:

a) detecting surface protein combinations of a protein network that are on the surface of the untreated tumor cells, whereby the protein network comprises up to 30 surface proteins selected from the group consisting of:

1. CD4	2. CD8	3. HLA-DR	4. HLA-DQ	5. CD3
6. CD26	7. CD38	8. CD45RA	9. CD16	10. CD57
11. CD56	12. CD7	13. CD54	14. CD58	15. CD138
16. CD13	17. CD62L	18. CD71	19. CD11b	20. CD36
21. CD29	22. CD49d	23. CD18	24. CD49f	25. CD19
26. CD2	27. CD20	28. CD10	29. CD44	30. CD80;

b) treating said or similar tumor cells with at least one potential inhibitor that is not directed against an aminopeptidase;

c) detecting the surface protein combinations of the protein network that are on the surface of the treated tumor cells; and

d) comparing the surface protein combinations detected in steps a) and c), whereby the at least one inhibitor, if there is a

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divergence of the surface protein combinations detected in step a) from the surface protein combinations detected in step c) in that there is at least one modification of a surface protein, will be suitable for blocking polarization of said tumor cells.

13. (Withdrawn) The method as claimed in claim 12 characterized in that said or similar tumor cells are also treated with at least one aminopeptidase inhibitor in step b), with the combination of the at least one inhibitor and the at least one aminopeptidase inhibitor, if there is a divergence of the surface protein combinations detected in step a) from the surface protein combinations detected in step c) in that there is at least one modification of a surface protein CD13, will cause blocking of polarization of the tumor cells and/or immune cells.

14. (Withdrawn) The method as claimed in claim 12 characterized in that said method includes a further step, following step d), in which the at least one aminopeptidase inhibitor identified in step d) or a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor is added to at least one polarizing tumor cell and/or immune cell, and the further development of the at least one polarizing tumor cell and/or immune cell is detected.

15. (Withdrawn) The method as claimed in claim 12 characterized in that said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells

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to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one inhibitor identified in step d) or with a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

16. (Canceled)

17. (Withdrawn) The method as claimed in claim 10 characterized in that said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one aminopeptidase inhibitor identified in step d) to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

18. (Withdrawn) The method as claimed in claim 13 characterized in that said method includes a further step, following step d), in which the at least one aminopeptidase inhibitor identified in step d) or a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor is added to at

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least one polarizing tumor cell and/or immune cell, and the further development of the at least one polarizing tumor cell and/or immune cell is detected.

19. (Withdrawn) The method as claimed in claim 13 characterized in that said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one inhibitor identified in step d) or with a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

20. (Withdrawn) The method as claimed in claim 14 characterized in that said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one inhibitor identified in step d) or with a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

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21. (Currently Amended) A pharmaceutical preparation for treatment of tumor diseases ~~which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 2~~, the preparation comprising:

an aminopeptidase inhibitor, wherein the inhibitor causes blocking of polarization of an invasive tumor cell by modifying at least one surface protein, wherein the surface protein is a member of a protein network on the surface of the invasive tumor cell, the protein network comprising proteins selected from the group consisting of CD4, CD8, HLA-DR, HLA-DQ, CD3, CD26, CD38, CD45RA, CD16, CD57, CD56, CD7, CD54, CD58, CD138, CD13, CD62L, CD71, CD11b, CD36, CD29, CD49d, CD18, CD49f, CD19, CD2, CD20, CD10, CD44 and CD80.

22. (Canceled)

23. (Currently Amended) ~~A~~ The pharmaceutical preparation of claim 21, the preparation further comprising an additional inhibitor ~~which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 4~~.

24. (Currently Amended) ~~A~~ The pharmaceutical preparation of claim 23, wherein the ~~which can be produced using at least one aminopeptidase inhibitor or a combination of at least one~~

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~~aminopeptidase inhibitor and at least one~~ additional inhibitor ~~as claimed in claim 5~~ causes blocking of polarization of an invasive tumor cell by modifying at least one surface protein that is not an aminopeptidase, wherein the surface protein is a member of a protein network on the surface of the invasive tumor cell, the protein network comprising proteins selected from the group consisting of CD4, CD8, HLA-DR, HLA-DQ, CD3, CD26, CD38, CD45RA, CD16, CD57, CD56, CD7, CD54, CD58, CD138, CD13, CD62L, CD71, CD11b, CD36, CD29, CD49d, CD18, CD49f, CD19, CD2, CD20, CD10, CD44 and CD80.

25. (Canceled)

26. (Canceled)

27. (New) The method of claim 4, wherein the additional inhibitor causes a modification of a surface protein of the invasive tumor cell, the surface protein being responsible for adhesion to an endothelial cell, an extracellular structure or any combination thereof.

28. (New) The method of claim 4, wherein the additional inhibitor is a homophthalimide, a actinonin, a bestatin, an antibody against one of said surface proteins or a combination thereof.

29. (New) The method of claim 1, wherein the at least one surface protein is CD13.

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30. (New) The pharmaceutical preparation of claim 21, wherein the at least one surface protein is CD13.

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